

scrFI
nciI
mspi
hpaII
dsav
sfaNI
fokI cauII
bstF5I
alul
acuI bssKI drdI
901 ACAGCTTGTC TGTAAAGCGGA TGCCGGGGAGC AGACAAGCCC GTCAGGGGCG GTTGGCGGGT GTCGGGGCGC AGCCATGACC CAGTCACGTA
TGTCGAACAG ACATTGCGCT ACGGCCCTCG TCTGTTGGG CAGTCCCGCG CAGTCGCCCA CAACGCCCA CAGCCCCGGG TCGGTACTGG GTCAGTGCAAT
901 GCGATAGCGG AGTTGGCTTA ACTATGCGGC ATCAGAGCAG ATTGTACTGA GAGTGCACCA TATGCGGTGT GAATACCGC ACAGATGCCG AAGGAGAAAA
CGTATCGCC TCAACCGAAT TGATACGCCG TAGTCTCGTC TAACATGACT CTCACGTGGT ATACGCCACA CTTTATGGCG TGTCTACGCA TTCCTCTTTT
101 TACCGCATCA GCGGCATTG GCCATTACAG CCGATTCAGG GTTGGGAAGG GCGATCGGTG CCGGCCTTCTT CGCTATTACG CCAGCTGGCG AAGGGGGGT
ATGGCGTAGT CCGCGGTAAG CGGTAGTCC GATGCGTTGA CAACCCCTCC CGCTAGCCAC GCGCGGAGAA GCGATATATG GGTGACCGC TTCCTCCCTA

FIG. 7FF

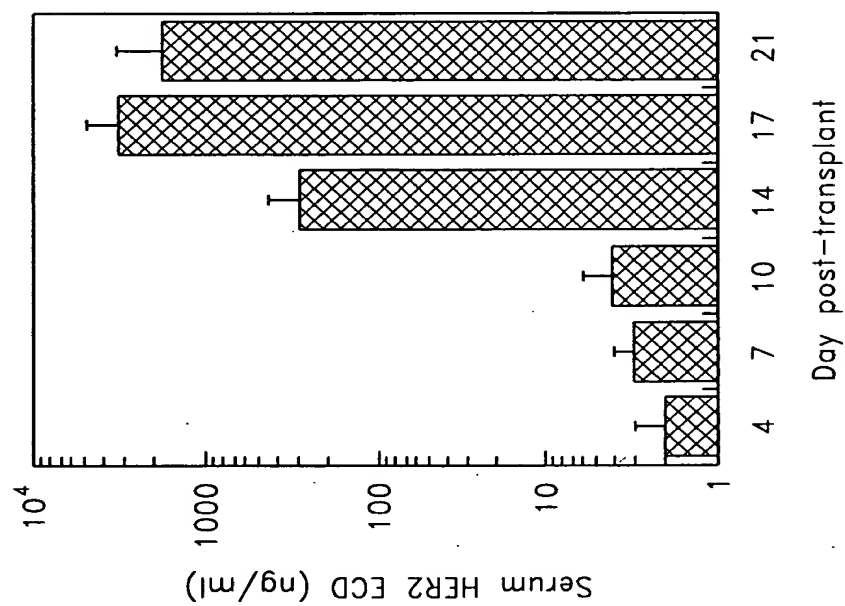


FIG. 8A

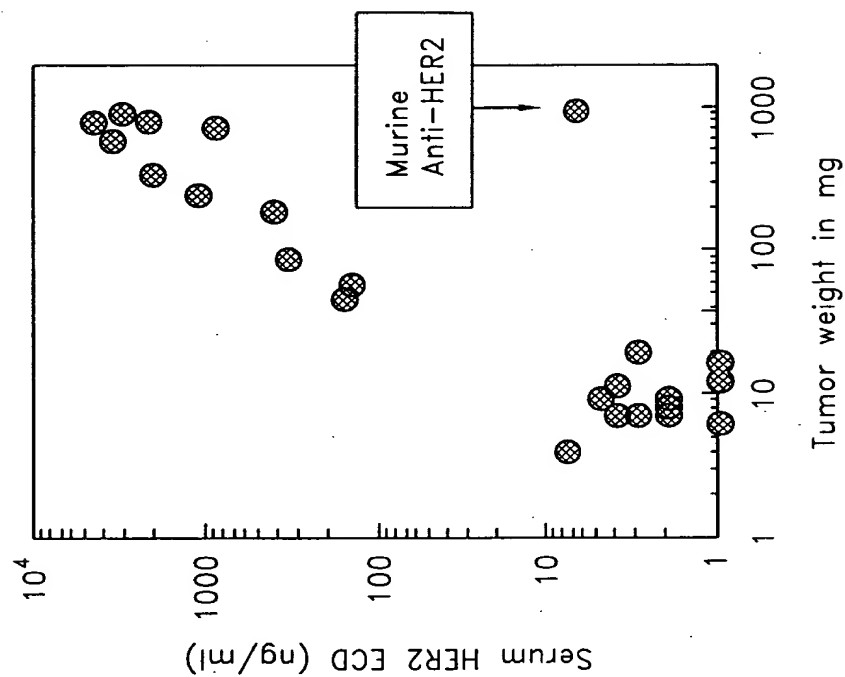


FIG. 8B

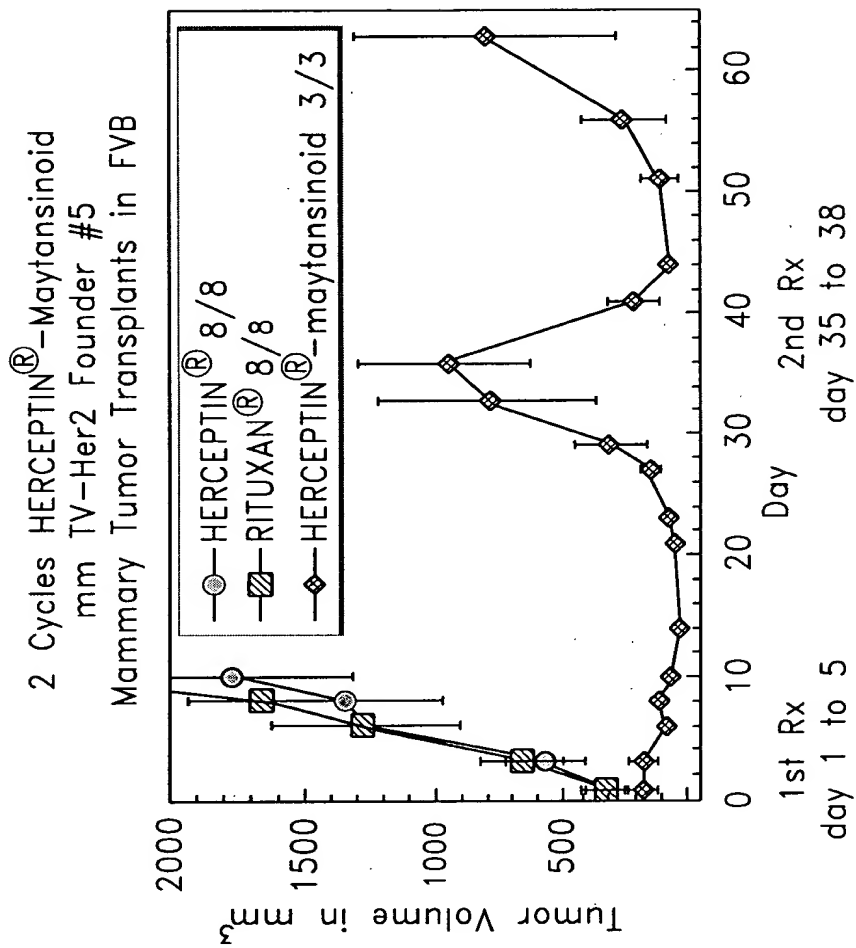


FIG. 9

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Both

FITC-Anti-

Control IgG

Label

HER2

HER3

HER4

HER5

HER6

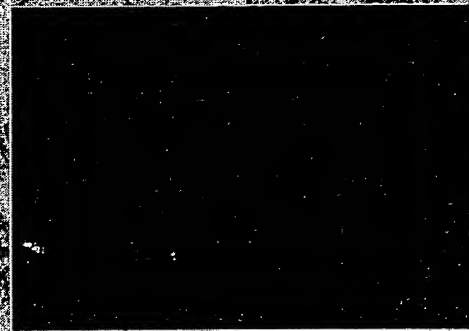
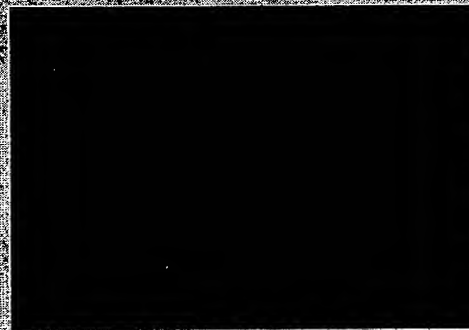
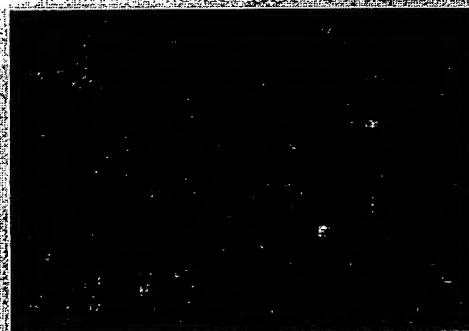
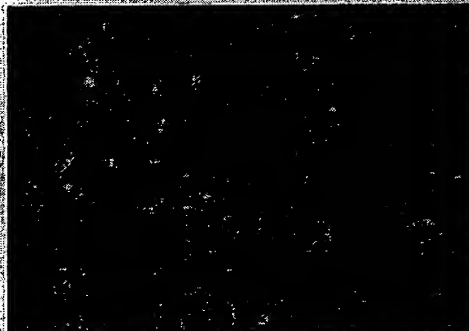
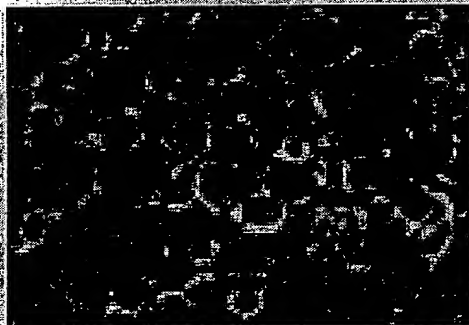
HER7

HER8

HER9

HER10

HER11



H1299

F05

wnt

p53^{-/-}

FIG. 10

FIG. 11

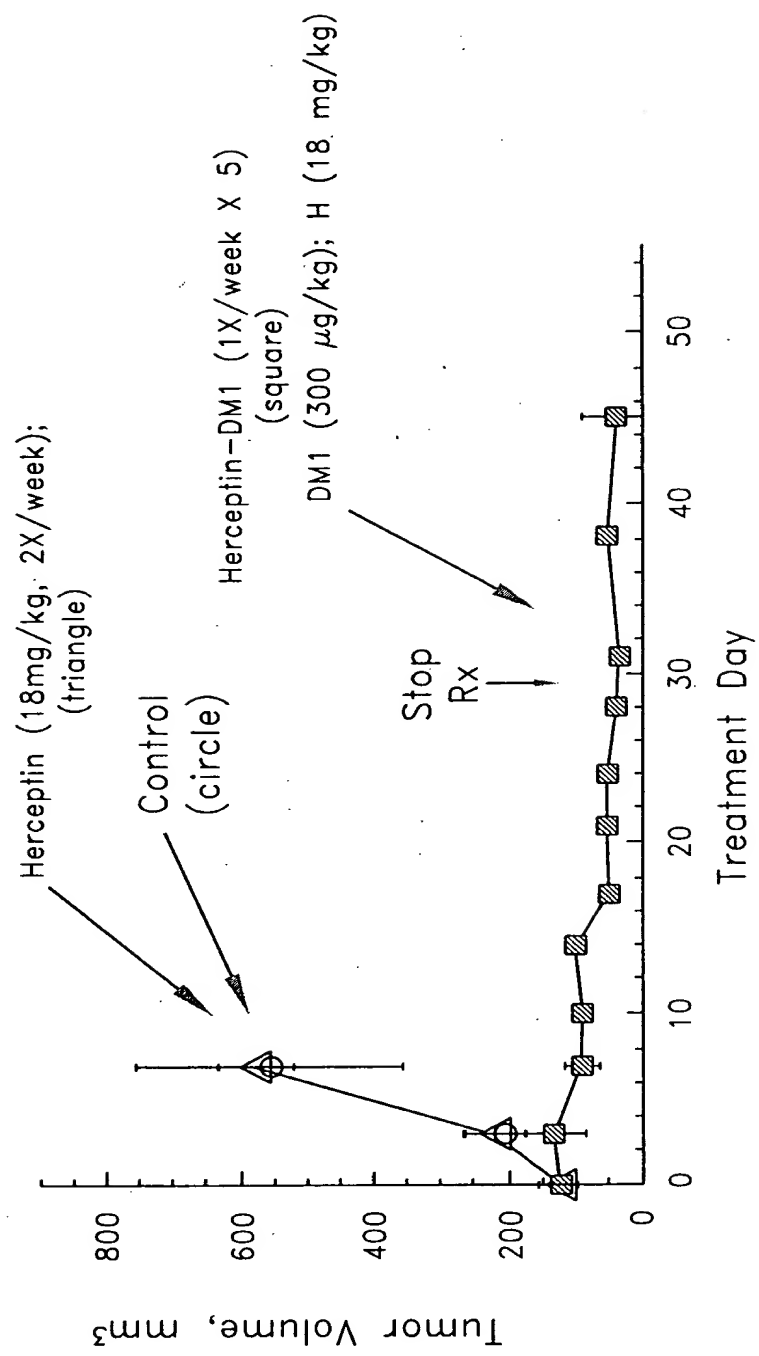


FIG. 11

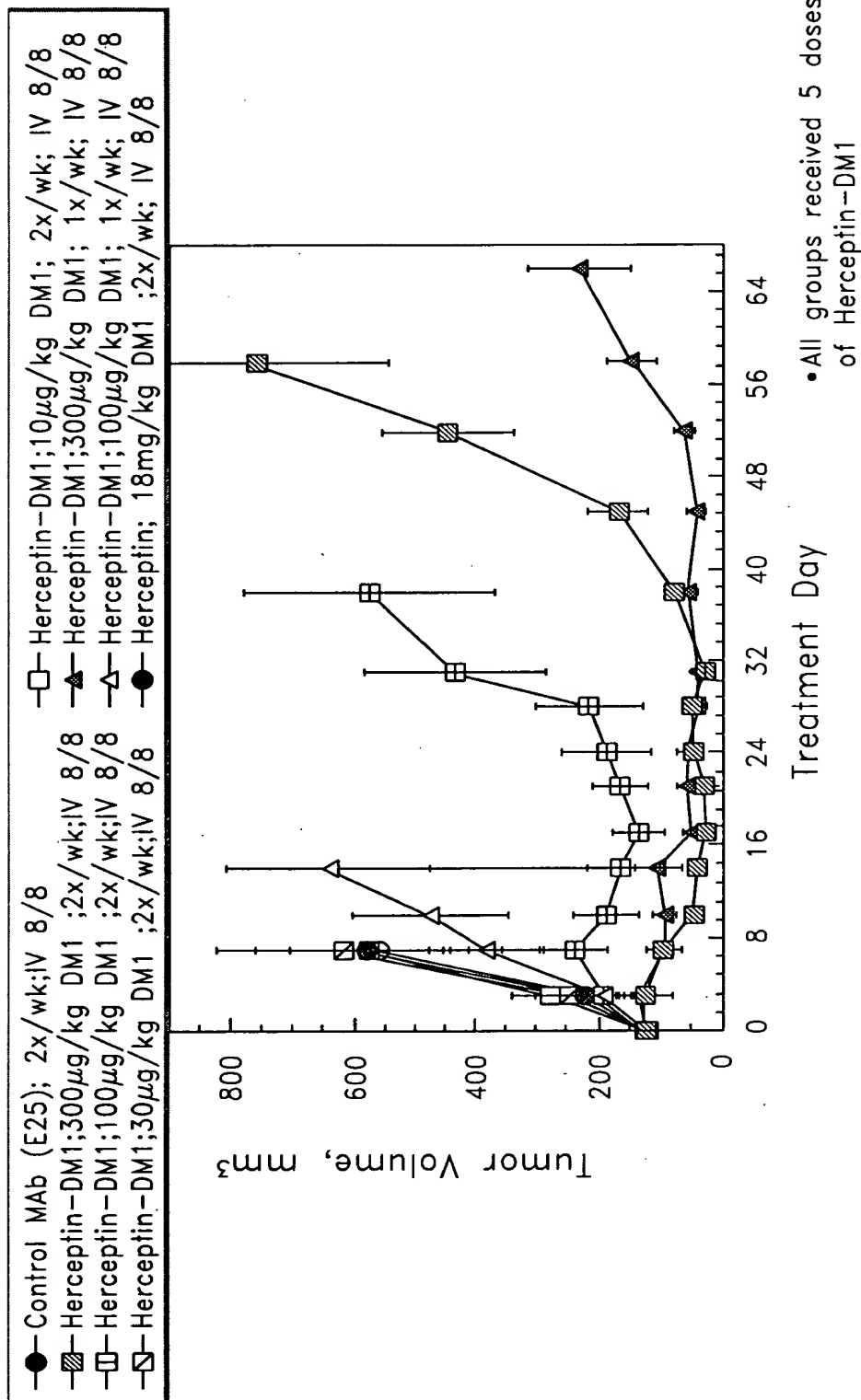


FIG. 12

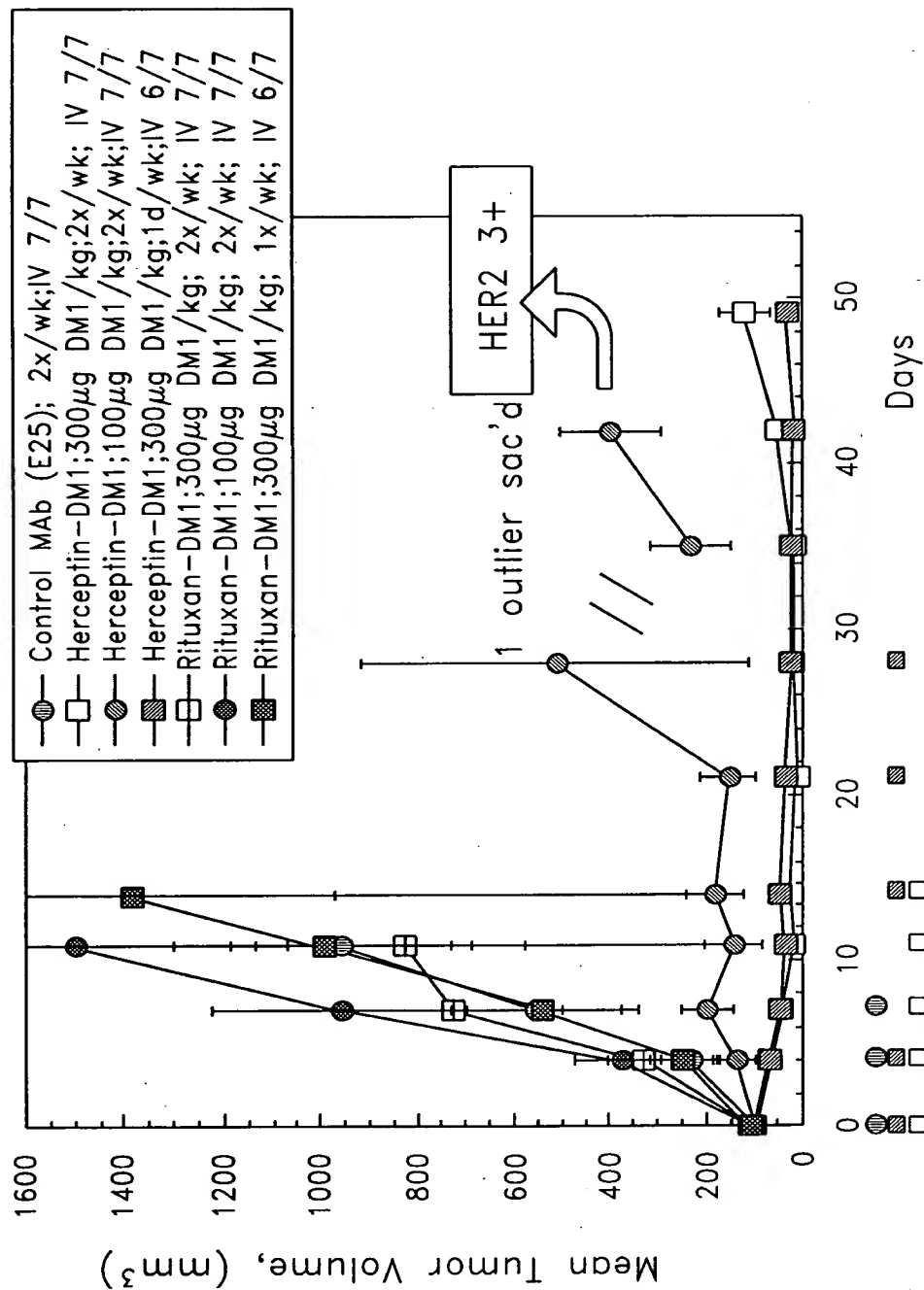


FIG. 13

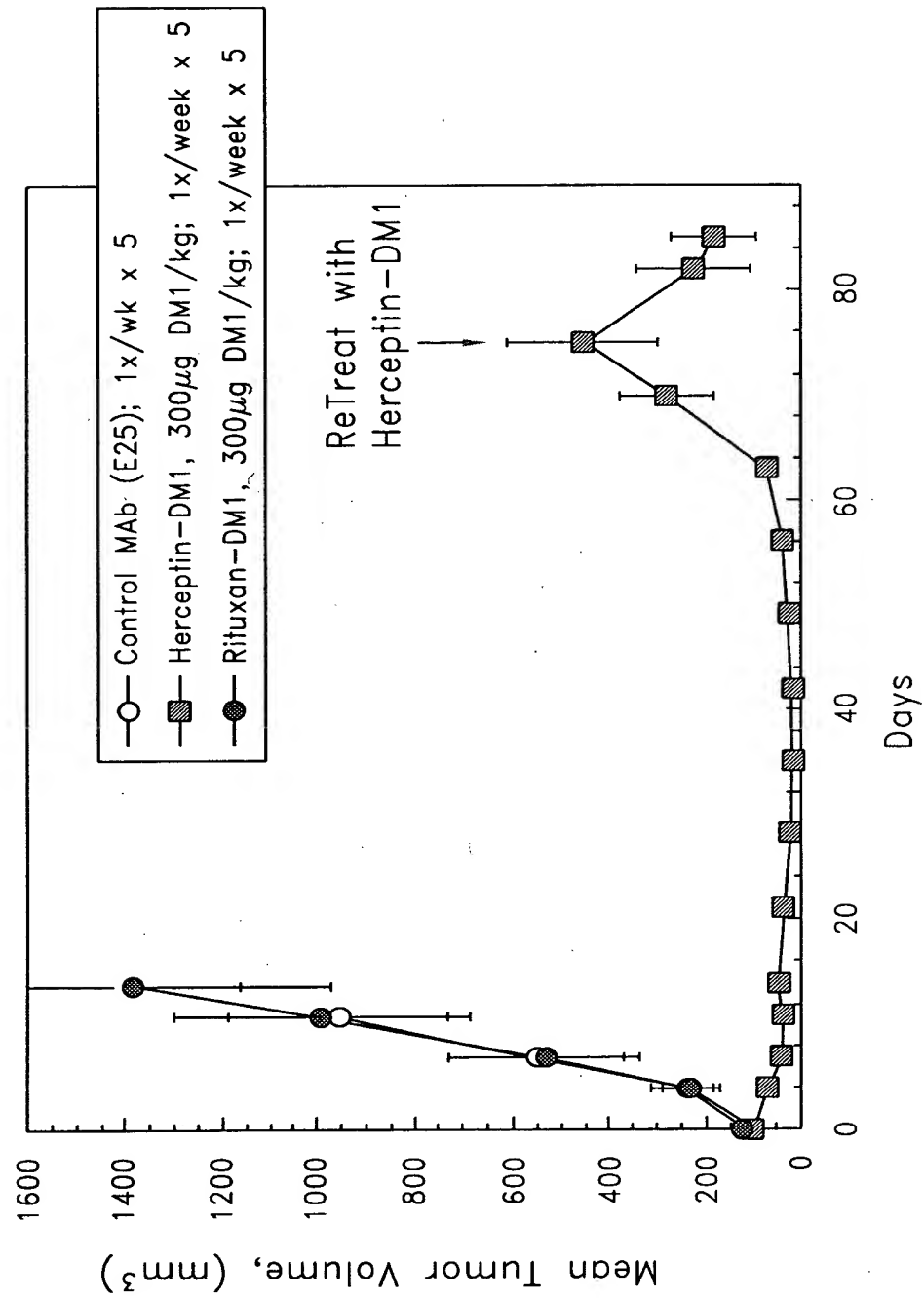


FIG. 14

5' -> 3' direction of the DNA sequence

rmaI
 maeI
 styI
 bsaJI
 blnI
 avrII
 haeIII/pal
 stuI
 haeI
 mnlI bfaI
 mnlI
 bseRI
 TTTGGAGGCC
 AAACCTCCGG

sau96I
 sau96I
 pspOMI/bsp120I
 nlaIV

hgiIII
 thal haeIII/palI
 fnuDII/mvnI
 sacII/sstII
 mspAII/nspBII
 kspI bsp1286
 dsaI bmyI
 bsaJI asuI
 fnu4HI/bsouI
 haeIII/palI
 mcrI banII
 eagI/smaII/eclXI
 eaeI cac8I
 cfrI acil

xhoI
 smlI
 pleI
 taqI taqI
 salI paeR7I
 claI/bsp106 hinfi
 aluI bspDI
 hindIII taqI
 accI avai
 scaI xbaI bsrBI acil apaI
 GAGCGGCGC GGGCGCCATCG CCTCTGACAG CAACGTCTAT GACCTCCTAA
 TAGCTATGCGC AGCTGAGCTC TCATGAAGAT CTCGCGGCGC CCGGGGTAGC GGAGACTGTC GTTGACAGATA CTGGAGGATT
 ATCCGAAAC GTTTTTCGAA
 ^start of BS insert of HER2 xba-hindIII
 ^end of human HER2 insert from BS at xhoI
 ^start of hgh ex 4 (cla/nar)
 ^TG PCR 5' pri

FIG. 7U

```

mspl
hpalI
scrFI
nciI
dsav
caulI
bssKI
bslI
tsei
fnu4HI/bsoFI
mnlI
mboII
bsrI
bgII
bstYI/xhoII
scfI
taqI
rmaI
maeI
bfal
sau96I
avaII
asul
fokI
bstF5I
ppuMI
mnlI
sfaNI
eco0109I/draII
701 AGGACCTAGA GGAAGGCATC CAAACGCTGA TGGGGAGGCT GGAAGATGGC AGCCCCCGGA CTGGGCAGAT CTTCAGCAG ACCTACAGCA AGTTCGACAC
TCCTGGATCT CCTTCCGPAG GTTTGCGACT ACCCCTCCGA CCTTCTACCG TCGGGGGCCT GACCCGCTA GAAGTTCGTC TGGATGTCGT TCAAGCTGTG
^end of ex 4/ start ex 5
801 AAACTCACAC AACGATGAC CACTACTCAA GAACTACGGG CTGCTCTACT GCTTCAGGAA GGACATGGAC AAGTCGAGA CATTCCTGCG CATCGTCGAC
TTTGAGTGTG TTGCTACTGC GTGATGAGTT CTTGATGCCC GACGAGATGA CGAAGTCTCTT CCTGTACCTG TTCCAGCTCT GTAAGGACGC GTAGCACGTC

```

FIG. 7V

[illegible][illegible]

FIG. 7X

המקור: המידע המוצג כאן הוא למטרות חינוך בלבד. אין להשתמש בו לצורכי רפואה או להחליט על טיפול. המידע אינו מהווה ייעוץ רפואי.

```

scrFI
mvaI
ecorII
ecorII
dsav
bstNI
bssKI
apyI
    sau3AI
    haeIII/palI
    mscI/balI
    haeI
    eaeI
    cfrI
        hphI
        301 GGGGTTTCAC CATATTGGCC AGGCTGGTCT CCAACTCCTA ATCTCAGGTG ATCTACCCAC CTGGCCCTCC CAATTTGCTG GGATTACAGG CGTGAACCAC
        CCCCAGAGTG GTATACCGG TCCGACAGA GGTGAGGAT TAGAGTCCAC TAGATGGTG GAACGGAGG GTTAACGAC CTAATGTCC GCACTTGGTG

        hphI
        401 TGCTCCCTTC CCTGTCCTTC TGATTTTAA ATAACTATAC CAGCAGGAGG AGTCCAGAC ACAGCATAGG CTACCTGCCA TGGCCCAACC GGTGGGACAT
        ACAGGGAAG GGACAGGAAG ACTAAATTT TATTGATATG GTCTGCTCTC TCGAGTCTG TCGGTATCC GATGAGCGGT ACCGGGTGG CCACCTGTA

        mspI
        cfrI01/bsrFI
        bsaWI
            styI sau96I hpaII
            ncoI haeIII/palI
            dsaI asuI ageI
            bsaJI pflMI
            bspMI nlaIII bslI
            bsmFI
            501 TTGAGTTGCT TGCTTGGCAC TGCTCTCTCA TGGGTTGGGT CCACTCAGTA GATGCTGTTT GAATTACGAT CGGTGCACAT TAATTCATGA AATTCGTAAT
            AACTCAACGA ACGAACCGTG ACAGGAGAGT ACGCAACCCA GGTGAGTCAT CTACGGACAA CTTAATGCTA GCCACGTGTA ATTAAGTACT TTAAGCATTA

            hgiAI/aspHI
            sau3AI
            mboI/ndeII tru9I
            dpnII bsp1286
            dpnI bsiHKAI tsp509I
            pvuI/bspCI mseI nlaIII
            mcrI bmyI aseI/asnI/vspI
            bsiEI apaII/snoI rcaI apoI
            tsp509I alw4I/snoI bspHI tsp509I
            501 TTGAGTTGCT TGCTTGGCAC TGCTCTCTCA TGGGTTGGGT CCACTCAGTA GATGCTGTTT GAATTACGAT CGGTGCACAT TAATTCATGA AATTCGTAAT
            AACTCAACGA ACGAACCGTG ACAGGAGAGT ACGCAACCCA GGTGAGTCAT CTACGGACAA CTTAATGCTA GCCACGTGTA ATTAAGTACT TTAAGCATTA

            ^start of linker 2
            ^end of linker 2

```

FIG. 7Y

[illegible]

FIG. 7AA

[illegible]

FIG. 7BB

tru9I nlaIV
 tsp509I hgiCI
 tru9I mnlI
 mseI mnlI
 ahaIII/draI maeIII mnlI
 701 CTTTAAATT AAAAATGAAG TTTTAAATCA ATCTAAAGTA TATATGAGTA AACTTGGTCT GACAGTTACC AATGCTTAAT CAGTGAGGCA CCTATCTCAG
 GAAAATTTAA TTTTACTTC AAAATTAGT TAGATTTCAT ATATACTCAT TTGAACCAGA CTGTCAATGG TTACGAATTA GTCACTCCGT GGATAGAGTC

 sau3AI bsrI tseI
 mboI/ndeII sau96I fnu4HI/bsoFI
 dpnII foki nlaIV bbvI
 dpnI bstF5I haeIII/palI
 801 CGATCTGTCT ATTTCTGTCA TCCATAGTTG CCTGACTCCC CGTCGTGTAG ATAATACGA TACGGGAGGG CTTACCATCT GGGCCAGTG CTGCAATGAT
 GCTAGACAGA TAAAGCAAGT AGGTATCAAC GGAAGTGGG GCAGCACATC TATTGATGCT ATGCCCTCCC GAATGGTAGA CCGGGGTAC GACGTACTA

 bsmAI
 bsai
 thai
 fnuDII/mvni mspI
 bstUI mwoI haeIII/palI sau96I foki
 bsh1236I hpaII sau96I hinPI avalI mnlI
 aciI hphI nlaIV cac8I hpaII asuI hhaI/cfoI asuI aciI bstF5I
 901 ACCGGGAGAC CCACGCTCAC CGGCTCCAGA TTTATCAGCA ATAAACCAGC CAGCCGGAAG GCGCGAGGCG AGAAGTGGTC CTGCAACTTT ATCCGCCCTCC
 TGGCGCTCTG GGTGGAGTG GCCGAGTCT TAATTGGTCT CCGGCTCGG TCTTACCAG GACGTTGAAA TAGGCGGAGG

 scrFI
 nciI
 mspI
 hpaII
 tsp509I dsav xmaI
 tru9I cauII maeI
 msel bssKI bfaI
 bsrI aseI/asnI/vsPI aluI
 001 ATCCAGTCTA TTAATTGTTG CCGGGAAGCT AGAGTAAGTA GTTCCGCCAGT TAATAGTTTG CGCAACGTTG TTGCCATTGC TGCTGGCATC GTGGTGTAC
 TAGGTACAGT AATTAACAAC GGGCCCTCGA TCTCATTCTA CAAGCGGTCA ATTATCAAC GGTGTGCAAC AACGTAACG ACAGCGGTAG CACCACACTG

FIG. 7CC

[illegible]

FIG. 7DD

sau96I
avaII
asuI
nlaIV
scrFI
draIII
mvaI
mwoI bspl286 bsmFI
bstAPI bmyI ecoRII
hgiAI/aspHI dsav
bspl286 nlaIV bstNI
bsiHKAI hgiCI bssKI
bmyI baniI bsaJI
apaLI/snoI apyI
alw44I/snoI bsaJI
381
458 L R E L G S G L A L I H H N T H L C F V H T V P W D Q
101 ACTGAGGGAA CTGGGCAGTG GACTGGCCCT CATCCACCAT AACACCCACC TCTGCTTCGT GCACACGGTG CCCTGGGACC
TGACTCCCTT GACCCGTCAC CTGACCGGA GTAGTGGTA TTGTGGGTGG AGACGAGCA CGTGTGCCAC GGGACCCCTGG T
491 Q A L L H T A N R P E D E C V G E G L A C H Q L C A R
sequence change from Coussens to Yamamoto

FIG. 7K

scrFI
 mvaI
 ecorII
 dsav
 bstNI
 bssKI
 apyI
 tseI
 fnu4HI/bsoFI
 bbvI
 draIII
 sau96I
 haeIII/palI
 asuI
 bsrI
 hincII/hindII
 bsgI
 pstI
 scfI
 haeIII/palI
 sau96I
 asuI
 nlaIV
 mnlI
 bsmI
 scaI
 mnlI
 bsaJI
 bmyI
 apyI
 dsav
 bstNI
 bssKI
 bsmI
 apyI
 bsaJI
 banII
 csp6I
 rsaI
 bsgI
 pstI
 scfI
 nlaIV
 bstNI
 dsav
 ecorII
 mvaI
 scrFI
 301 GGCCCAACCA GTGTGTCAAC TGCAGCCAGT TCCTTCGGG CCAGGAGTGC GTGAGGAAT GCCGAGTACT GCAGGGGCTC CCCAGGGAGT ATGTGAATGC
 CCGGGTGGT CACACAGTTG ACGTCGGTCA AGGAAGCCCC GGTCCTCAGC CACCTCCTTA CGGCTCATGA CGTCCCGGAG GGTCCCTCA TACACTTACG
 525 P T Q C V N C S Q F L R G Q E C V E E C R V L Q G L P R E Y V N A

tspRI
 mwoI
 bstAPI
 alwNI
 alw26I/bsmAI
 ddeI
 ddeI
 bslI
 ddeI
 tspRI
 maeIII
 tsp45I
 bsaWI
 sau96I
 avall
 asuI
 mnlI
 bslI
 bsrI
 pflMI
 tspRI
 haeIII/palI
 haeI
 bmyI
 bslI
 GTCCGTGACA AACGGCACGG TGGGACTCAC AGTCGGGGTC TTACCGAGTC ACTGGACAAA ACCTGGCCTC CGACTGGTCA CACACCGGAC ACGGGTGATA
 558 R H C L P C H P E C Q P Q N G S V T C F G P E A D Q C V A C A H Y

tseI
 mwoI
 fnu4HI/bsoFI
 mspAlI/nspBII
 acil
 cac8I
 sau96I
 haeIII/palI
 acil
 mspAlI/nspBII
 mnlI
 sau96I
 nlaIV
 avall
 asuI
 ppuMI
 eco0109I/draII
 mwoI
 asuI
 bbvI
 mspAlI/nspBII
 mnlI
 nspHI
 nspI
 cac8I
 mnlI
 hinPI
 cac8I
 bseRI
 hhaI/cfoI
 AGATGAGGAG GCGCATGCC
 TTTCTGGGAG GGAAGACGCA CCGGGCGACG GGTGCGCCAC ACTTTGGACT GGAGAGGATG TACGGGTAGA CTTCAAAGG TCTACTCCTC CCGCGTACGG
 591 K D P P F C V A R C P S G V K P D L S Y M P I W K F P D E E G A C Q

FIG. 7L

3601 AGCCTTGCCC CATCACTGC ACCCACTCCT GTGTGGACCT GGATGACAAG GGCTGCCCGG CCGAGCAGAG AGCCAGCCCT CTGACGTCCA TCCTCTCTGC
 TCGGAACGGG GTAGTTGACG TGGGTGAGGA CACACCTGGA CCTACTGTTC CCGACGGGGC GGCTCGTCTC TCGTGGGA GACTGCAGGT AGCAGAGACG
 625 P C P I N C T H S C V D L D D K G C P A E Q R A S P L T S I V S A

scrFI	tail	esp3I
mvaI	maeiI	
ecorII	hinfI/acyI bsmAI	
dsaV	ahaiI/bsaHI	
bstNI		
bssKI		
apyI		
sau96I	tseI	
avaII foki	fnu4HI/bsoFI	
asuI bstF5I	bbvI aciI	
mslI	cac8I mnlI aatII bsmBI aciI	

mspI	mspI	
mroI	mroI	
bspMII	bspMII	
bspEI	bspEI	
bsaWI	bsaWI	
sau3AI	sau3AI	
mboI/ndeII	mboI/ndeII	
dpnII	dpnII	
dpnI	dpnI	
alwI	alwI	
nlaIV	nlaIV	
bstYI/xhoII	bstYI/xhoII	
bamHI	bamHI	
alwI	alwI	
bsmI	bsmI	
GGTGGTTGGC ATTCTGCTGG TCCTGGTCTT GGGGGTGGTC TTTGGGATCC TCATCAAGCG ACGGAGCAG AGATCCGGA AGTACACGAT GCGGAGACTG	tseI	mwoI
CCACCAACCG TAAGACGACC AGCACCAGAA CCCCACCAAG AAACCTAGG AGTAGTTCC TGCCTGCTGC TTCTAGGCTC TCATGTGCTA CGCCTCTGAC	fnu4HI/bsoFI hpaII rsaI	aciI
658 V V G I L L V V V L G V V F G I L I K R R Q Q K I R K Y T M R R L	bbvI mboII accIII csp6I sfaNI bsmAI bbvI	

FIG. 7M

[illegible]

bslI
sau3AI
mboI/ndeII
dpnII
dpnI
alwI
nlaIV
bstYI/xhoII
bamHI
sfaNI
accI
alwI
bstYI/xhoII
hhaI/cfoI
hlnPI
mwoI
mboI/ndeII
dpnII
dpnI
bstYI/xhoII
hhaI
accI
sfaNI
alwI
bamHI
bstYI/xhoII
nlaIV
alwI
dpnI
dpnII
mboI/ndeII
sau3AI
bslI

mscI/balI
haeI
eaeI
tspRI
tsp509I cfrI mslI
apoI bsrI haeIII/palI
mnlI

901 AGGTGCTGG ATCTGGCGCT TTTGGCACAG TCTACAAGGG CATCTGGATC CCTGATGGGG AGAATGTGAA AATTCAGTG GCCATCAAAG TGTTGAGGGA
TCCACGAACC TAGACCGCGA AAACCGTGTC AGATGTTCCC GTAGACTAG GGAATACCC TCTTACACTT TTAAGGTGTC CGGTAGTTT ACAACTCCCT

725 V L G S G A F G T V Y K G I W I P D G E N V K I P V A I K V L R E

	001	758
AAACACATCC	CCCAAAGCCA	ACAAAGAAAT
CTTAGACGAA	GCATACGTGA	TGGCTGGTGT
GGGCTCCCCA	TATGTCTCCC	GCCTTCTGGG
CATCTGCCTG		
TTTGTGTAGG	GGGTTTCGGT	TGTTTCTTTA
GAATCTGCTT	CGTATGCACT	ACCGACCACA
CCCGAGGGGT	ATACAGAGGG	CGGAAGACCC
GTAGACGGAC		
NTSPKAN	K E I L D E A Y V M	A G V G S P Y V S R L L G I C L

FIG. 7N

[illegible]

FIG. 70

4601 ATGTTGGATG ATTGACTCTG AATGTCGGCC AAGATTCCGG GAGTTGGTGT CTGAATTCTC CCGCATGGCC AGGACCCC AGCGTTTGT GGTCCATCCAG
TACAACCTAC TAACTGAGAC TTACAGCCGG TTCTAAGGCC CTCACCCACA GACTTAAGAG GGCTACCGG TCCCTGGGG TCGCGAAACA CCAGTAGGTC
958 C W M I D S E C R P R F R E L V S E F S R M A R D P Q R F V V I Q

4701 AATGAGGACT TGGGCCAGC CAGTCCCTTG GACAGCACCT TCTACCGCTC ACTGCTGGAG GACGATGACA TGGGGGACCT GGTGGATGCT GAGGAGTATC
TTACTCCTGA ACCCGGTCG GTCAGGGAAC CTGTCGTGGA AGATGGCGAG TGACGACCTC CTGCTACTGT ACCCCCTGGA CCACCTACGA CTCCTCATAG
991 N E D L G P A S P L D S T F Y R S L L E D D M G D L V D A E E Y L

4601 ATGTTGGATG ATTGACTCTG AATGTCGGCC AAGATTCCGG GAGTTGGTGT CTGAATTCTC CCGCATGGCC AGGACCCC AGCGTTTGT GGTCCATCCAG
TACAACCTAC TAACTGAGAC TTACAGCCGG TTCTAAGGCC CTCACCCACA GACTTAAGAG GGCTACCGG TCCCTGGGG TCGCGAAACA CCAGTAGGTC
958 C W M I D S E C R P R F R E L V S E F S R M A R D P Q R F V V I Q

FIG. 7Q

4901 TGGTACCCCA GCAGGGCTTC TTCTGTCCAG ACCCTGCCCC GGGCGTGGG GGCATGGTCC ACCACGAGCA CCGCAGCTCA TCTACCAGGA GTGGCGGTGG
 1025 V P Q Q G F F C P D P A P G A G G M V H R H R S S S T R S S G G G

4901 TGGTACCCCA GCAGGGCTTC TTCTGTCCAG ACCCTGCCCC GGGCGTGGG GGCATGGTCC ACCACGAGCA CCGCAGCTCA TCTACCAGGA GTGGCGGTGG
 1025 V P Q Q G F F C P D P A P G A G G M V H R H R S S S T R S S G G G

4901 TGGTACCCCA GCAGGGCTTC TTCTGTCCAG ACCCTGCCCC GGGCGTGGG GGCATGGTCC ACCACGAGCA CCGCAGCTCA TCTACCAGGA GTGGCGGTGG
 1025 V P Q Q G F F C P D P A P G A G G M V H R H R S S S T R S S G G G

FIG. 7R


```

1  AAGCTCGATC GGTGCACATT AATTCATGAT CGCGAGCTAG CAGCTTGAT GCCTGCAGCA GAAATGGTTG AACTCCCGAG AGTGTCTTAC ACCTAGGGGA
   TTCGAGCTAG CCACGTGTAA TTAAGTACTA GCGCTCGATC GTCGAACGTA CGGACGTCGT CTTTACCAAC TTGAGGGCTC TCACAGGATG TGGATCCCCC
   *start of linker 1
   *end of linker 1
   *start of MMTV promoter

   hgiAI/aspHI   sau3AI   rmaI
   mboI/ndeII   mboI/ndeII   maeI
   dpnII   bsp1286   tru9I   dpnII   nheI   nlaIII   tseI   rmaI
   pvuI/bspCI   mseI   nlaIII   thalI   cac8I   nsphI   fnu4HI/bsoFI   maeI
   mcrI   bsiHKAI   tsp509I   fnuDII/mvnI   cac8I   nsphI   bsvI   bfaI
   bsiEI   bmyI   asel/asnI/vspI   bstUI   bfaI   aluI   nspl   pstI   styI
   taqI   apaLI/snoI   rcaI   bsh1236I   fnu4HI/bsoFI   cac8I   scfI   bsaJI
   aluI   dpnI   alw44I/snoI   bspHI   nruI   aluI   bsvI   cac8I   bsgI   blnI
   1  AAGCTCGATC GGTGCACATT AATTCATGAT CGCGAGCTAG CAGCTTGAT GCCTGCAGCA GAAATGGTTG AACTCCCGAG AGTGTCTTAC ACCTAGGGGA
   TTCGAGCTAG CCACGTGTAA TTAAGTACTA GCGCTCGATC GTCGAACGTA CGGACGTCGT CTTTACCAAC TTGAGGGCTC TCACAGGATG TGGATCCCCC
   *start of linker 1
   *end of linker 1
   *start of MMTV promoter

   styI   hgiJII
   bsaJI   bsp1286
   tseI   hinPI
   fnu4HI/bsoFI   hhaI/cfoI
   bsvI   mstI   bsnII
   styI   bcoI   aviIII/fspI   foki   mwOI
   bsaJI   ahdI/eam1105I   bstF5I   tseI
   fnu4HI/bsoFI   fnu4HI/bsoFI   bsvI   fnu4HI/bsoFI
   bsvI   bsvI

101 GAAGCAGCCA AGGGGTTGTT TCCACCAAG GACGACCCCGT CTGCGCACAA ACAGATGAGC CCATCAGACA AAGACATATT CATTCTCTGC TGCAAACTTG
    CTTCGTCCGT TCCCCAACAA AGGGTGGTTC CTGCTGGGCA GACGCGTGT TGCCTACTCG GGATAGTCTGT TTCTGTATAA GTAAGAGACG ACGTTTGAAC

   mwOI   hgiJII   mboII
   cac8I   hgiJII   earI/ksp632I
   hgiAI/aspHI   bsp1286   bmyI   pleI   tru9I   sapi   mamI
   bsp1286   bsiHKAI   bmyI   banII   hphI   hinfi   msel   aluI   bsaBI
   mwOI   acil   mwOI   bmyI   banII   hphI   hinfi   msel   aluI   bsaBI
   aluI   GCATAGCTCT GCTTTGCTGG GGCATTTGGG GAAGTTGCGG TTCGTGCTCG CAGGGCTCTC ACCCTTGACT CTTTAAATAG CTCTTCTCTG CAAGATTACA
   CGTATCGAGA CGAAACGACC CCGTAACCCC CTTCAACGCC AACACGAGC GTCCCGAGAG TGGGAACCTGA GAAAATTATC GAGAAGACAC GTTCTAATGT

```

FIG. 7A

[illegible]

FIG. 7B

[illegible]

FIG. 7C

501 CACCTATTGG TCTTACTGAC ATCCACTTTG CCTTCTCTCTC CACAGGTGC CACTCCCAGG TTCAATTACA GCTCTTAAGC GGCGCAAGC TTGATATCGA
GTGGATAACC AGAATGACTG TAGGTGAAAC GGAAGAGAG GTGTCCACAG GTGAGGGTCC AAGTTAATGT CGAGAATTTCG CCGCGCTTCG AACTATAGCT

501 CACCTATTGG TCTTACTGAC ATCCACTTTG CCTTCTCTCTC CACAGGTGC CACTCCCAGG TTCAATTACA GCTCTTAAGC GGCGCAAGC TTGATATCGA
GTGGATAACC AGAATGACTG TAGGTGAAAC GGAAGAGAG GTGTCCACAG GTGAGGGTCC AAGTTAATGT CGAGAATTTCG CCGCGCTTCG AACTATAGCT

^end of chimeric intron at pCI 989

end of BS insert at HindIII^

501 CACCTATTGG TCTTACTGAC ATCCACTTTG CCTTCTCTCTC CACAGGTGC CACTCCCAGG TTCAATTACA GCTCTTAAGC GGCGCAAGC TTGATATCGA
GTGGATAACC AGAATGACTG TAGGTGAAAC GGAAGAGAG GTGTCCACAG GTGAGGGTCC AAGTTAATGT CGAGAATTTCG CCGCGCTTCG AACTATAGCT

^end of chimeric intron at pCI 989

end of BS insert at HindIII^

sau96I
 avall
 asul
 nlaIV
 scrFI
 nciI
 mspI
 hpaII
 dsav
 cauII
 bssKI
 hhaI/cfoI
 mwoI
 hinPI
 hhaI/cfoI
 1701 GCGCCCTCCC AGCCGGGTCC AGCCGGAGCC ATGAGCTGG CGGCCTTGTG CCCTCTCTCG CCTCTTGGC CCCCAGAGCC GCGAGCACCC
 CGCGGAGGG TCGGCCCTCG TCGGCCCTCG M E L A A L C R W G L L L A L L P P G A A S T Q
 1
 hgiAI/aspHI
 bsp1286
 bsiHKAI
 cac8I
 thaI
 fnuDII/mvni
 bstUI mslI
 bsh1236I
 aciI bmyI
 fnu4HI/bsoFI
 mspAI/nspBII mnlI
 bmyI bseRI
 banII mnlI
 fnu4HI/bsoFI bseRI
 fnu4HI/bsoFI
 haeIII/palI
 aluI aciI
 cac8I
 bstXI
 bsaJI
 aluI
 nlaIV
 dsav
 cauII
 bssKI
 hhaI/cfoI
 mwoI
 hinPI
 hhaI/cfoI
 1701 GCGCCCTCCC AGCCGGGTCC AGCCGGAGCC ATGAGCTGG CGGCCTTGTG CCCTCTCTCG CCTCTTGGC CCCCAGAGCC GCGAGCACCC
 CGCGGAGGG TCGGCCCTCG TCGGCCCTCG M E L A A L C R W G L L L A L L P P G A A S T Q
 1

mspI
 cfr10I/bsrFI
 hgiAI/aspHI
 bsp1286
 bsiHKAI
 mslI
 bmyI hpaII
 apaLI/snoI
 alw44I/snoI
 1801 AAGTGTGCAC CGGCACAGAC ATGAAGCTGC GGCTCCCTGC CAGTCCCGAG ACCACCTGG ACATGCTCCG CCACCTCTAC CAGGCTGCC AGGTGGTGCA
 TTCACACGTG GCGGTGTCTG TACTTCGAC CCGAGGGAGC GTACGGGTC TGGGTGGACC TGTACGAGGC GGTGGAGATG GTCCCGACGG TCCACACGT
 25 V C T G T D M K L R L P A S P E T H L D M L R H L Y Q G C Q V V Q
 scrFI
 mval
 ecorII
 dsav
 bstNI
 bssKI
 apyI
 tseI
 mnlI bssKI tseI
 ecorII bsaJI fnu4HI/bsoFI
 scrFI
 mval
 ecorII
 dsav
 bstNI
 bssKI
 apyI
 tseI
 mnlI bssKI tseI
 ecorII bsaJI fnu4HI/bsoFI

scrFI
 mval
 ecorII
 dsav
 bstNI
 bssKI
 apyI
 hphI bspMI
 cac8I
 sbfI ecorV apyI
 1901 GGGAAACCTG GAACCTACCT ACCTGCCAC CAATGCCAGC CTGTCTCTCC TGCAGGATAT CAGGAGGTG CAGGCTTACG TGCTCATCGC TCACAACCAA
 CCTTTGGAC CTTGAGTGA TGGACGGGTG GTTACGGTGC GACAGGAGG ACCTCTATA GGTCTCCAC GTCCCGATGC ACAGTAGCG AGTGTGGTT
 58 G N L E L T Y L P T N A S L S F L Q D I Q E V Q G Y V L I A H N Q
 hgiAI/aspHI
 bsp1286
 bsiHKAI
 bmyI
 tail
 maelI
 bsaAI
 mnlI
 scrFI
 mval
 ecorII
 dsav
 bstNI
 bssKI
 sse8387I
 sbfI ecorV apyI
 cac8I
 sbfI ecorV apyI
 1901 GGGAAACCTG GAACCTACCT ACCTGCCAC CAATGCCAGC CTGTCTCTCC TGCAGGATAT CAGGAGGTG CAGGCTTACG TGCTCATCGC TCACAACCAA
 CCTTTGGAC CTTGAGTGA TGGACGGGTG GTTACGGTGC GACAGGAGG ACCTCTATA GGTCTCCAC GTCCCGATGC ACAGTAGCG AGTGTGGTT
 58 G N L E L T Y L P T N A S L S F L Q D I Q E V Q G Y V L I A H N Q

FIG. 7F

hinPI
 hhaI/cfoI
 thaI
 fnuDII/mvnl
 bstUI
 mwoI bsh1236I mspI
 hpaII mwoI
 cfr10I/bsrFI
 301 GCCTGCCACC CCTGTTCTCC GATGTGTAAG GGCTCCCGCT GCTGGGGGAGA GAGTTCTGAG GATTGTGAGA GCCTGACGCG CACTGTCTGT GCCGGTGGCT
 CGGACGGTGG GGACAAGAGG CTACACATTC CCGAGGGCGA CGACCCCTCT CTCAAGACTC CTAACAGTCT CGGACTGGC GTGACAGACA CGGCCACCGA
 191 A C H P C S P M C K G S R C W G E S S E D C Q S L T R T V C A G G C C
 mspAII/nspBII
 mwoI tseI
 nlaIV fnu4HI/bsoFI
 hgiJII bslI
 bsp1286 bbvI
 bmyI aciI
 banII bslI
 cac8I
 301 GCCTGCCACC CCTGTTCTCC GATGTGTAAG GGCTCCCGCT GCTGGGGGAGA GAGTTCTGAG GATTGTGAGA GCCTGACGCG CACTGTCTGT GCCGGTGGCT
 CGGACGGTGG GGACAAGAGG CTACACATTC CCGAGGGCGA CGACCCCTCT CTCAAGACTC CTAACAGTCT CGGACTGGC GTGACAGACA CGGCCACCGA
 191 A C H P C S P M C K G S R C W G E S S E D C Q S L T R T V C A G G C C
 tseI
 fnu4HI/bsoFI
 mspAII/nspBII
 bslI
 aciI
 cac8I
 bsp1286
 bmyI bbvI
 401 GTGCCCCGCTG CAGGGGCCA CTGCCCCACTG ACTGCTGCCA TGAGCAGTGT GCTGCCGGCT GCACGGGCC CAGCACTCT GACTGCCCTGG CCTGCCTCCA
 CACGGGCGAC GTTCCCGGT GACGGGTGAC TGACGACGGT ACTCGTCACA CGACGGGCCA CGTGCCCGG GTTCGTGAGA CTGACGGACC GGACGGAGGT
 225 A R C K G P L P T D C C H E Q C A A G C T G P K H S D C L A C L H
 sau96I
 nlaIV
 haeIII/palI
 sau96I
 pspOMI/bsp120I
 nlaIV
 hgiJII
 eco109I/draII
 mspI
 hpaII
 nael/ngoMI bmyI
 cfr10I/bsrFI asuI
 cac8I
 banII
 tseI fnu4HI/bsoFI
 fnu4HI/bsoFI asuI
 bbvI nlaIII tspRI
 bbvI bbvI apaI
 401 GTGCCCCGCTG CAGGGGCCA CTGCCCCACTG ACTGCTGCCA TGAGCAGTGT GCTGCCGGCT GCACGGGCC CAGCACTCT GACTGCCCTGG CCTGCCTCCA
 CACGGGCGAC GTTCCCGGT GACGGGTGAC TGACGACGGT ACTCGTCACA CGACGGGCCA CGTGCCCGG GTTCGTGAGA CTGACGGACC GGACGGAGGT
 225 A R C K G P L P T D C C H E Q C A A G C T G P K H S D C L A C L H
 haeIII/palI
 haeI
 scrFI
 mval
 ecoRII
 dsaV
 bstNI
 bssKI
 apyI
 mwoI cac8I mnli
GACTGCCCTGG CCTGCCTCCA
 CTGACGGACC GGACGGAGGT

FIG. 7H

xcmI sau3AI scrFI sau96I
 scrFI mboI/ndeII mvaI nlaIV
 mvaI dpnII ecoRII avaiI
 ecoRII dpnI dsav asuI
 dsav bstYI/xhoII bstNI sanDI
 bstNI fnu4HI/bsaFI bssKI ppuMI
 bssKI bglII mboII nlaIV
 apyI cac8I mboII ecoO109I/draII
 apyI mboII nlaIV bsmFI mnII tspRI
 801 CAGTGCCAAT ATCCAGGAGT TTGCTGGCTG CAAGAAGATC TTTGGGAGCC TGGCATTTCT GCCGGAGAGC TTTGATGGG ACCCAGCCTC CAACACTGCC
 GTCACGGTTA TAGGTCTCA AACGACCGAC GTTCTTCTAG AAACCTCTCG ACCGTAAGA CGGCTCTCG AAACCTACCC TGGGTGGAG GTTGTGACGG
 358 S A N I Q E F A G C K K I F G S L A F L P E S F D G D P A S N T A

 aluI bpmI/gsuI tseI mspI
 bsrBI fnu4HI/bsaFI fnu4HI/bsaFI hpaII
 aciI mwoI bbvI haeIII/palI
 901 CCGCTCCAGC CAGAGCAGCT CCAAGTGTTT GAGACTCTGG AAGAGATCAC AGGTTACCTA TACATCTCAG CATGGCCGGA CAGCCTGCCT GACCTCAGCG
 GCGAGGTCG GTCTCGTCGA GGTTCACAAA CTCTGAGACC TTCTCTAGTG TCCAATGGAT ATGTAGAGTC GTACCGGCCT GTCCGACGGA CTGGAGTCGC
 391 P L Q P E Q L Q V F E T L E E I T G Y L Y I S A W P D S L P D L S V

 hinPI hhaI/cfoI
 hhaI/cfoI nlaIV
 nlaIV narI
 narI kasi
 kasi hinII/acyI
 hinII/acyI hgiCI
 hgiCI haeII
 haeII tsp509I
 tsp509I ecoRI
 ecoRI apoI
 apoI ahaII/bsaHI mwoI bslI
 ahaII/bsaHI mwoI bslI
 001 TCTTCCAGAA CTTGCAAGTA ATCCGGGAC GAATTCTGCA CAATGGCGCC TACTCGCTGA CCCTGCAAGG GCTGGGCATC AGCTGGCTGG GGCTGGCTC
 AGAAGGTCTT GGACGTTTCAAT TAGGCCCCCTG CTTAAGACGT GTTACCGCGG ATGAGCGACT GGGACGTTCC CGACCCGTAG TCGACCGACC CCGACGCGAG
 425 F Q N L Q V I R G R I L H N G A Y S L T L Q G L G I S W L G L R S

FIG. 7J

VARIABLE HEAVY DOMAIN

	10	20	30	40	
2C4	EVQLQQSGPELVKPGTSVKISKAS	[GFTFTDYTMD]	WVKQS	*	
	** ** *	** ** *		*	
574	EVQLVESGGGLVQPGGSLRLSCAAS	[GFTFTDYTMD]	WVRQA		
		** * *			
hum III	EVQLVESGGGLVQPGGSLRLSCAAS	[GFTFSSYAMS]	WVRQA		
	50	a	60	70	80
2C4	HGKSLEWIG	[DVNPNSSGGSIYNQRFKG]	KASLTVDRSSRIVYM		
	* *	**	*** *	**** *	
574	PGKGLEWVA	[DVNPNSSGGSIYNQRFKG]	RFTLSVDRSKNTLYL		
		*****	*** ** *		
hum III	PGKGLEWVA	[VISGDGGSTYYADSVKG]	RFTISRDNKNTLYL		
	abc	90	100ab	110	
2C4	ELRSLTFEDTAVYYCAR	[NLGPSFYFDY]	WGQGTTLTVSS		
	*** **		**		
574	QMNSLRAEDTAVYYCAR	[NLGPSFYFDY]	WGQGTTLTVSS		

hum III	QMNSLRAEDTAVYYCAR	[GRVGYSLYDY]	WGQGTTLTVSS		

FIG. 1

Variable Light Domain

	10	20	30	40
2C4	DTVMTQSHKIMSTVGDRVSITC	[KASQDVSIGVA]	WYQQRP	*
	**	**** *		
574	DIQMTQSPSSLASVGDRVITIC	[KASQDVSIGVA]	WYQQKP	
		* ** ***		
hum KI	DIQMTQSPSSLASVGDRVITIC	[KASQDVSIGVA]	WYQQKP	
	50	60	70	80
2C4	GQSPKLLIY [SASYRYT]	GVDRFTGSGSGTDF	FTISSVQA	
	**	* *	* *	
574	GKAPKLLIY [SASYRYT]	GVPSRFSGSGSGTDF	TLTISSLQP	
		* ****		
hum KI	GKAPKLLIY [AASSLES]	GVPSRFSGSGSGTDF	TLTISSLQP	
	90	100		
2C4	EDLAVYYC [QQYIYIPYT]	FGGKTKLEIKRT		
	*	*		
574	EDFATYYC [QQYIYIPYT]	FGQGTKVEIKRT		
		*** *		
hum KI	EDFATYYC [QQYNSLPWT]	FGQGTKVEIKRT		

FIG. 2

Maytansinoids
(DM1)

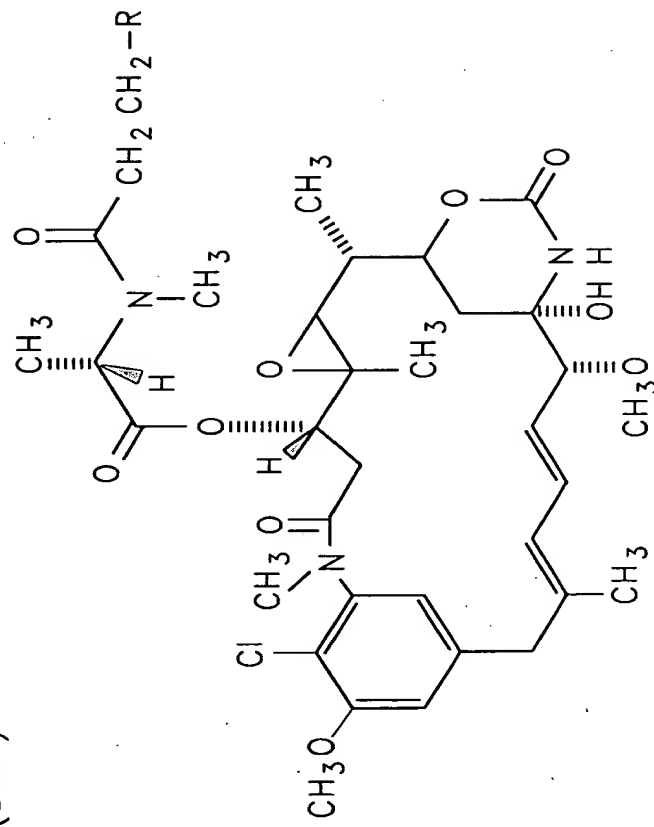


FIG. 3

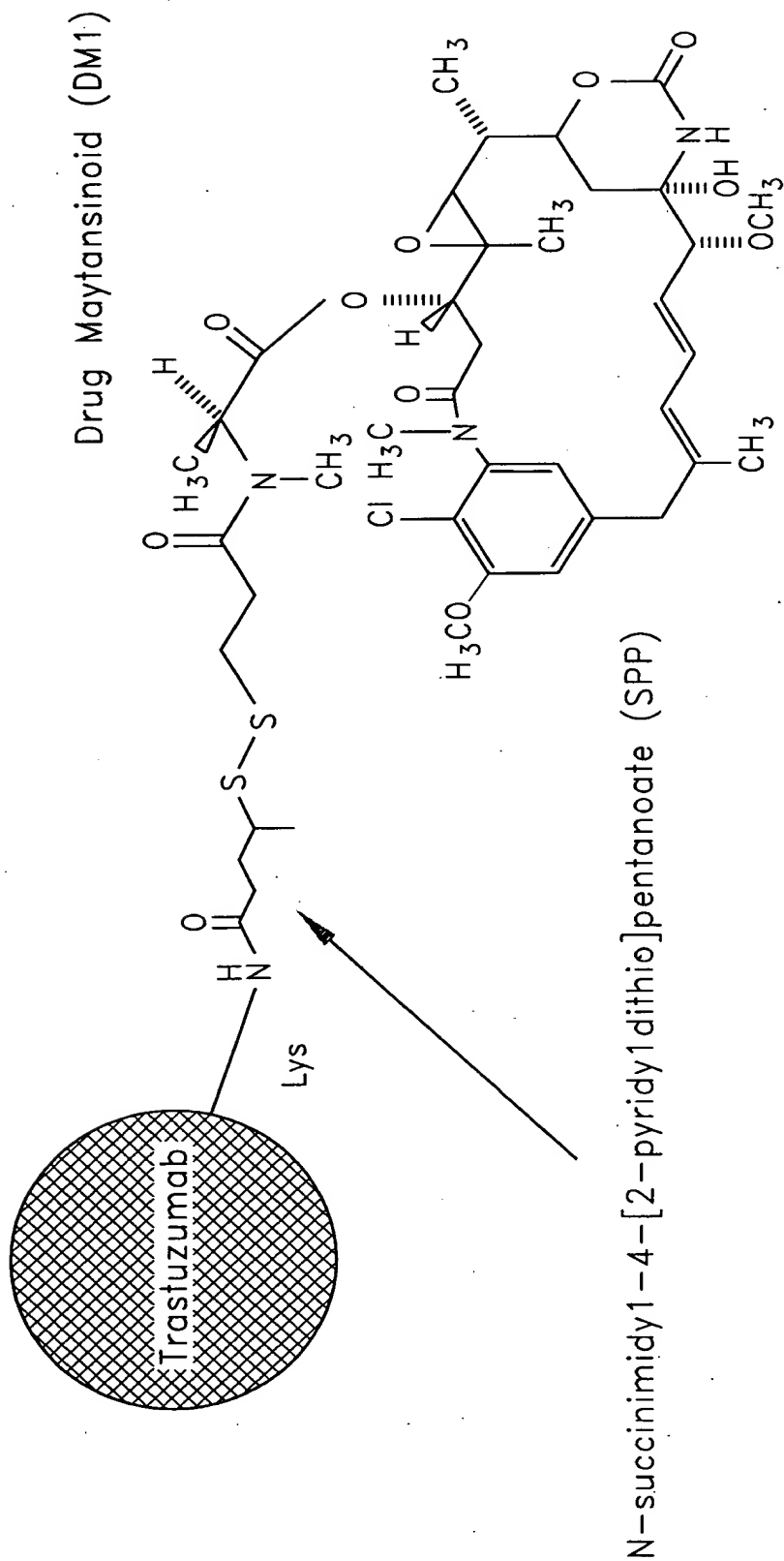


FIG. 4

HERCEPTIN[®] DM1

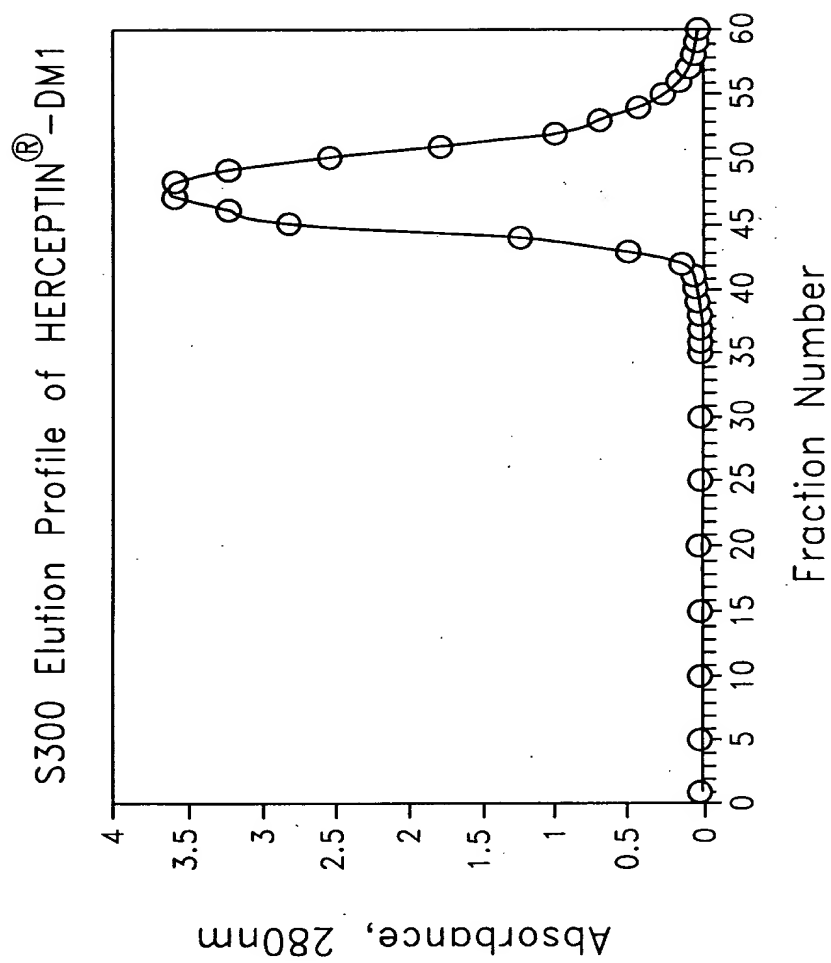


FIG. 5

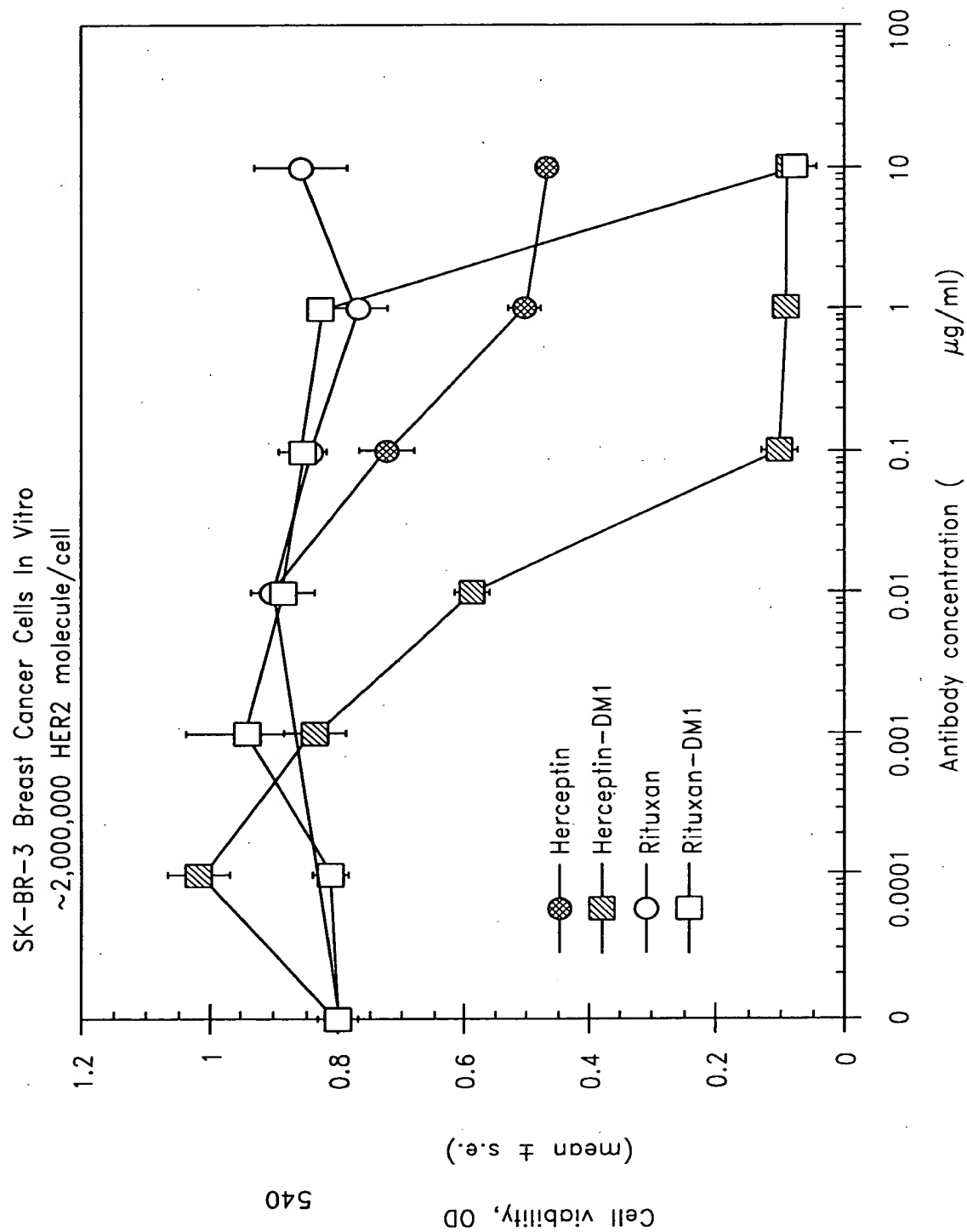


FIG. 6